

**REMARKS—General**

By the above amendment, Applicant has amended the title to emphasize the key element of the invention. Applicant has also amended a paragraph in specification to restate the term: incubator/shaker. According to the suggestions in the Office Action of Nov. 30, 2005, Applicant has also rewritten all claims to reduce the scope of the base claim and define the invention more specifically so as to overcome the rejections.

Most rewritten claims are related to the previous claims. In order to easily compare NEW claims with CANCELED claims, their relationship is listed in a following Table I.

Table I

<b>NEW Claims</b>	<b>CANCELED Claims</b>
24.	1., 2., 8 and 9. (modified combination)
25.	3. (modified)
26.	4., 5. and 17. (modified combination)
27.	13., 15. and 18. (related)
28.	7. (modified)
29.	23. (modified)
30.	10. (modified)
31.	11. (modified)
32.	11. (modified)
33.	(NEW) (described in paragraph [020])
34.	19. and 20. (modified)
35.	2., 12., 14. and 16. (modified combination)
36.	13., 15. and 18. (modified combination)
37.	7. (related)
38.	17. (modified)
39.	(NEW) (described in paragraph [020])

40.	19. (modified)
41.	19. (related)
42.	11. (related)
43.	11. (related)
44.	(NEW) (mentioned in paragraph [01] & [02] )
45.	22. (modified)

### **The References and Differences of the Present Invention**

Applicant will make discussion on the references and the novelty of the present invention and its unobviousness over the references.

**U.S. Pat. No. 4314029—Ohtake** et al. describes an apparatus that utilizing optical absorption spectrum method for measuring the concentration change of dissolved gases within a closed vessel. This reference does NOT disclose any apparatus or methods for monitoring biological cell concentration within the closed vessel. It would be obvious to one having ordinary skill in the art at that time that the optical apparatus with transmission (zero-angle light scattering) method described in the reference does NOT work for monitoring biological cell concentration if the light path through biological medium is too long and cell concentration is high that is true for cell culture. Therefore the apparatus described in Fig. 6 of the reference will not work for monitoring cell concentration if the vessel has a large volume such as over 100ml. To overcome this problem with a large volume vessel, the present invention utilizes a large angle scattering detection method. Furthermore the apparatus described in the reference is NOT designed for a shaking environment such as in an incubator/shaker.

**U.S. Pat. No. 6573991—Debreczeny** et al. describes a sensor comprises multiple radiation sources and multiple detectors for biomass concentration detection. The sensor is designed for applications with a bioreactor or a fermenter with a large volume of culture medium. The reference does NOT disclose any apparatus or

methods for monitoring biological culture in a shaking environment of an incubator/shaker. Furthermore the sensor would NOT work for monitoring the cell culture in a shaking environment when light reflection from air-medium interface becomes a critical problem if the incident light path is not carefully arranged. For the sensor in the reference, the volume of culture medium in a bioreactor is assumed to be large enough so that there is no culture medium boundary issue around the optical sensing area. However the boundary of a shaking culture medium in an incubator/shaker becomes a critical variable for an optical sensing technique because of limited culture medium volume with a shaking environment.

**U.S. Pat. No. 6653150—Reed** describes an apparatus that utilizing light scattering method for detecting average particle masses, static dimensions and other properties within an optical transparent vessel. However this reference DOES NOT disclose the light scattering method for monitoring particle concentration within the vessel because of the difficulty of making calibration with relative reference solution in the vessel. Furthermore the apparatus described in the reference is NOT designed for the shaking environment.

**The present invention has its unobviousness over the references.**

The diode laser with monochromic wavelength makes fluorescence detection possible. Importantly the high light intensity from a diode laser rather than a LED greatly increases the signal to noise ratio and the detection dynamic range of the cell culture monitoring apparatus particularly in a shaking culture environment of an incubator/shaker. Furthermore only in recent years, high quality, low cost and tiny diode lasers make the present invention technically and economically feasible.

Erlenmeyer flasks are popular and well known for the flask culture in an incubator/shaker. The conical shape of an Erlenmeyer flask prevents biological culture medium from possible spilling over under a shaking condition. However it may not be obvious in the art so far that the aeration for some cell culture especially bacteria culture requires a small volume of culture medium in a flask. Under a

shaking condition, such small volume culture medium driven by a centrifugal force usually appears and rotates around the bottom corner of the flask. Furthermore ambient light, bubbles, air-medium interface reflection and non-uniform scattering effects in the turbulent culture medium make great challenge to cell concentration measurement with an optical technique. These unique problems solved by the present invention were never before even recognized. In the present invention, an Erlenmeyer flask appears to be an ideal existing culture container for the light scattering detection technique. Its bottom corner with an angle less than 90 degree can make the culture medium less spread out under a shaking condition so that the light path can be made short without going through the air-medium interface.

## **CONCLUSION**

Applicant submits that the specification and claims are now in proper form, and that the claims all define patentably over the prior art. Therefore this application is now in condition for allowance.

### **Conditional Request for Constructive Assistance.**

Applicant has amended the specification and claims of this application so that they are proper, definite, and define novel feature that is also unobvious. If this application is not believed, for any reason, to be in full condition for allowance, applicant respectfully request the constructive assistance and suggestions of Examiner in order that applicant can place this application in allowable condition as soon as possible.

Very respectfully,



Hong Peng

42874 Via Navarra

Fremont, CA 94538

Tel: (510) 676 9606

Email: hong\_p127@yahoo.com